UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,263	09/28/2005	Toshihiro Nakashima	NAKASHIMA=6	3356

1444 7590 12/08/2010

Browdy and Neimark, PLLC
1625 K Street, N.W.
Suite 1100
Washington, DC 20006

EXAMINER	
OGUNBIYI, OLUWATOSIN A	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
12/08/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,263	NAKASHIMA ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-8,16,17,21 and 23* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☒ Claim(s) *6-7,16 and 17* is/are allowed.

6)☒ Claim(s) *8 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 9/29/10 has been entered into the record. Claims 1-5, 9-15, 18-20 and 22 has been cancelled. Claims 6-8, 16-17 and 21 have been amended. Claims 6-8, 16-17, 21 and 23 are pending in the application. Claims 6-8, 16-17, and 21 are under examination. Claim 23 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Objections/Rejections Withdrawn

The objection to claim 21 is withdrawn.

The rejection of claims 1-9 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment to the claims.

The rejection of claims 1-3 and 9 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the cancellation of the claims.

The rejection of claims 1-9 and 11-17 under 35 U.S.C. 112, first paragraph is withdrawn in view of the amendment to the claims.

The rejection of claim 21 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment to the claim.

The rejection of claims 11 and 22 under 35 U.S.C. 112, second paragraph is withdrawn in view of the cancellation of the claims.

The rejection of claims 1-2, 9, 11 and newly applied to new claim 22 under 35 U.S.C. 102(b) as being clearly anticipated by Sasaki et al. EP 1055429 A1 published 11/29/2000 is withdrawn in view of the cancellation of the claims.

The rejection of claims 1-3 and 9 under 35 U.S.C. 102(b) as being clearly anticipated by Nishi et al (The Journal of Immunology, 1997, 1558:247-254) is withdrawn in view of the cancellation of the claims.

The rejection of claims 1-2, 9, 11 and newly applied to claim 22 under 35 U.S.C. 102(b) as being clearly anticipated by Kappler et al. WO93/14634 Aug. 5 1993 is withdrawn in view of the cancellation of the claims.

Claim Rejections Maintained
Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claim 21 under 35 U.S.C. 112, first paragraph because the specification, while being enabling for modified SEB mutant N23Y wherein Asn at 23 position in the amino acid sequence of SEB as shown in SEQ ID NO: 1 is substituted with Tyr or modified SEB mutant 47-C-7 wherein the amino acid sequence of SEB at position 226-229 as shown in SEQ ID NO: 1 is Ala Thr Thr Gln or modified SEB mutant 47-C-1 wherein the amino acid sequence of SEB at position 226-229 as shown in SEQ ID NO: 1 is Lys Arg Ile Ile, that retains a therapeutic effect to rheumatoid arthritis or collagen induced arthritis;

does not reasonably provide enablement for retaining a therapeutic effect to rheumatoid arthritis or any other immunopathy equivalent to naturally occurring SEB. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

The facts that should be considered in determining whether a specification is enabling or if it would require an undue amount of experimentation to practice the invention include 1) the quantity of experimentation necessary to make or use the invention based on the content of the disclosure, (2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 735 (Fed. Cir.1988). The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737,

8 USPQ2d at 1404. While the analysis and conclusion of a lack of enablement are based on these factors discussed in MPEP § 2164.01(a) and the evidence as a whole, the factors that weigh more in making the instant enablement rejection were discussed in the previous action and as set forth below.

Nature of the invention and breadth of the claims

The nature of the instant invention is the use of the instantly claimed modified Staphylococcus Enterotoxin B (SEB). The specification teaches that intended use is for prophylactics or remedies for immunopathy such as rheumatoid arthritis, allergic disease etc. See p. 1 of the specification. The instant specification does not define immunopathy. The dictionary definition of immunopathy includes any abnormal immune response i.e. a deficient or absent immune response (e.g. combined immunodeficiency), excess production of gamma globulins, over-reaction to extrinsic antigens as in immediate and delayed type hypersensitivity and over-reaction to intrinsic antigens e.g. autoimmune diseases such as lupus erythematosus and thyroiditis (Definition of Immunopathy cited previously: http://medical-dictionary.thefreedictionary.com/immunopathy) The specification also states that immunopathy can be rheumatoid arthritis or allergic diseases (see p. 1 lines 11-12 of specification).

The claim requires that the modified SEB retain a therapeutic effect to immunopathy equivalent to naturally occurring SEB.

Guidance in the specification and the presence or absence of working examples

The teachings of the specification are limited to inhibition of symptoms in an animal model of rheumatoid arthritis i.e. mice collagen induced arthritis by administering a modified SEB N23Y mutant or modified SEB with the N23Y mutation in combination with the mutations at position 226-229. See construction and isolation of mutants on p. 19- 22, p. 23 table 1. Briefly, mice were given type II collagen twice to induce arthritis then said mice were administered the modified SEB. See p. 26-27 and figure 1. The specification on p. 27 and figure 6 teaches that the N23Y, the 47-C-7 and 4-C-1 mutants reduced symptoms of arthritis. In addition, this example showed that arthritis symptoms were treated in mice *having* arthritis with particular modified SEB.

The specification however does not correlate the equivalency of the therapeutic effect of the modified SEB to rheumatoid arthritis with the therapeutic effect of naturally occurring SEB to rheumatoid arthritis. There is no comparison of the therapeutic effect to any type of immunopathy of the modified SEB to the therapeutic effect of natural SEB to any immunopathy.

The specification teaches that the disclosed modified SEBs had proliferation activity on PBMCs (p. 23-24) and induced inhibitory cytokines at higher levels and induced inflammatory cytokines at lower levels relative to wild type SEB (p. 25). The specification does not correlate the cytokine inducing pattern of the modified SEBs disclosed in the specification with treatment of immunopathy equivalent to that of naturally occurring SEB.

The specification only provides guidance as to the therapeutic effect of the modified SEB to rheumatoid arthritis using the mouse collagen induced arthritis model however, it is not clear that the therapeutic effect is equivalent to that of the therapeutic effect to any immunopathy of natural SEB.

The state of the prior art

As to the use of the instant modified SEB that retains a therapeutic effect to immunopathy equivalent to that of naturally occurring SEB, natural SEB are secreted proteins that exhibit highly potent lymphocyte transforming mitogenic activity directed towards T cells and they cause massive immune responses that are non-specific and detrimental (Llewelyn et al. 2002 The Lancet Infectious Diseases 2: 156-162, cited previously) and this T cell activating mechanism of natural SEB has been harnessed for the treatment or killing of tumor cells (Forsberg et al WO 03/002143 A1 Jan. 9, 2003, cited previously). Forsberg et al teaches modified Staphylococcal enterotoxins having superantigen activity are used to make conjugates to treat tumors). The specification does not teach which other therapeutic effect is retained by the instantly claimed modified SEBs except for rheumatoid arthritis and collagen induced arthritis in the mice model and does not teach that the therapeutic effect of modified SEB including the only disclosed therapeutic effect for rheumatoid arthritis and collagen induced arthritis equivalent to that of natural SEB e.g. such as for treating cancers or for treating other immunopathies. The specification teaches that the disclosed modified SEBs had proliferation activity on PBMCs (p. 23-24) and induced inhibitory cytokines at higher levels and induced inflammatory cytokines at lower levels relative to wild type SEB (p. 25). Since the cytokine profile of the modified SEBs and that of natural SEB are different, it is unpredictable that the modified SEB will retain therapeutic effect equivalent to that of natural SEB for treatment of immunopathy such as rheumatoid arthritis, cancers or autoimmune diseases such as lupus erythematosus and thyroiditis.

In view of the nature of the invention, the breadth of the claims, the unpredictability of the retention of therapeutic effect to immunopathy of the instant modified SEB equivalent to natural SEB due to the different cytokine profiles of the modified SEB and the natural SEB, the state of the prior art, the

guidance in the specification as to the only disclosed therapeutic effect of modified SEB for rheumatoid arthritis and collagen induced arthritis and the lack of working example and guidance as to the equivalency of the therapeutic effect of modified SEB to any immunopathy with naturally occurring SEB, the specification is only enabling for use of the instantly claimed modified SEB mutants for treating rheumatoid arthritis and collagen induced arthritis but not enabled for the retention of a therapeutic effect to any immunopathy equivalent to that of naturally occurring SEB.

New Claim Rejections

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 8 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 4 of copending Application No. 12/644952 ('952). Although the conflicting claims are

not identical, they are not patentably distinct from each other because the '952 claim discloses a modified Staphylococcal enterotoxin B (SEB) wherein Asn at residue position 23 as shown in SEQ ID NO: 1 of the instant claim 8 is substituted with Tyr. Said modifies SEB inherently has reduced reactivity with a neutralizing antibody to SEB.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Status of Claims

Claims 8 and 21 are rejected. Claims 6-7 and 16-17 are allowable. Claim 23 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is (571)272-9939. The examiner can normally be reached on M-F 5:30 am- 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patricia Duffy can be reached on 571-272-0855. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Examiner, Art Unit 1645